PATENT SPECIFICATION (11) 1 502 144

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(54) AZOLE ANTIMYCOTICS IN COSMETICS

(71) We, BAYER AKTIENGESELLSCHAFT, a body corporate organised under the laws of Germany, of Leverkusen, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to the use of largely known azole antimycotics as cosmetics, especially as additives to hair toiletries.

The use of azole derivatives as medicaments is already known (compare, inter alia, Belgian Patent Specification 720,801, Belgian Patent Specification 741,310, U.S. Patent 3,737,548, German Offenlegungsschrift (German Published Specification) 1,911,646, Belgian Patent Specification 750,724, German Offenlegungsschrift (German Published Specification) 2,016,839, German Offenlegungsschrift (German Published Specification) 2,044,621, German Offenlegungsschrift (German Published Specification) 2,053,080, Belgian Patent Specification 778,973, Belgian Patent Specification 804,092 and Arzneimittelforschung 2, volume 21/1971, page 256—257).

Further, various agents intended to combat cosmetically objectionable or pathological changes in the scalp and hair are already known.

Thus, pyridone derivatives, such as 1-hydroxy-2-pyridones, are used as anti-dandruff agents (compare German Offenlegungsschrift (German Published Specification) 2,234,009) or salicyclic acid derivatives, such as the 2-ethyl-1,3-hexanediol ester of salicyclic acid, are recommended for combating dandruff and seborrhoea (compare U.S. Patent 2,523,867).

An itch-suppressant action in seborrhoeic conditions has been described for crotonyl-N-ethyl-o-toluidine [compare O. Saipt, Wiener med. Wschr. *102*, 413 (1952)].

F. Asbeck has reported on combating microsporiosis with triphenyl-dodecyl-phosphonium bromide [compare Z. Haut- and Geschlechtskrankheiten *14*, 117 (1956)].

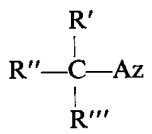
It is also known that colloidal sulphur is effective in cases of seborrhoea, dandruff, acne and infections [compare A. J. Wojwod, J. gen Microbiol. *10*, 509 (1954)].

The preparations comprising colloidal sulphur necessarily contain polythionic acids which according to clinical data are effective in cases of seborrhoea and acne [compare J. R. Delaney et al., J. Michigan St. Med. Soc. *50*, 1236 (1951)]. However, a disadvantage of the polythionates is their great instability.

In addition, the effect of all agents against Pityrosporum ovale, a blastomycete which must be regarded as one of the principal causes of pathological changes in the skin, especially in the scalp, is not always satisfactory, or is even non-existent.

It has now been found that certain azole compounds extensively known as azole antimycotics show a powerful action against all the skin changes caused, or partially caused, by *Pityrosporum ovale*. Surprisingly, this action is far more powerful and intense than was to be expected from the state of the art.

According to the present invention we provide a hair or skin toiletry composition comprising at least one azole antimycotic which is active against skin changes wholly or partially caused by *Pityrosporum ovale* and which have the formula (I):—



(I)

wherein Az is an optionally substituted imidazole or triazole group connected to the carbon atom by a nitrogen atom, and

R′, R″ and R‴ are independently selected from hydrogen atoms, optionally substituted phenyl groups, optionally substituted heterocyclic groups having O, S or N as a hetero atom, optionally-substituted aliphatic groups, optionally-substituted alicyclic groups, ester, ether, alkinyl, keto, hydroxy, amido and amino groups or

R′ and R″ together represent two optionally-substituted phenyl groups linked together by a bridging atom or group,

or a salt thereof, dispersed in a dermatologically acceptable carrier which contains a detergent-active compound and/or a perfume.

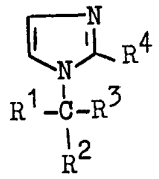
The invention specifically provides a shampoo composition comprising at least one azole antimycotic of the formula (I) and a dermatologically acceptable detergent active compound.

The compositions of the invention preferably contain from 0.05 to 5% by weight of the azole antimycotic, and the shampoo compositions preferably contain up to 30% by weight of the detergent active compound.

The basic skeleton of the azole compounds used in the present invention consists of a central carbon atom with an optionally substituted azole radical (imidazole or triazole). The remaining substituents on the carbon atom can be: optionally substituted phenyl, it being possible for two phenyl rings to be linked to one another (for example via $-(CH_2)_n-$, $-CH=CH-$, O or S, resulting, for example, in fluorene, dibenzocycloheptane or (thio)-xanthene derivatives); five-membered or six-membered, optionally substituted heterocyclic structures with N, O or S as the hetero-atom; aliphatic acyclic or alicyclic radicals; functional groups, such as, for example, ester, ether, alkinyl, alkenyl, keto, hydroxyl or amino groups.

The following may be mentioned as examples of the active compounds used according to the invention (compare Tables 1 to 13):

Table 1

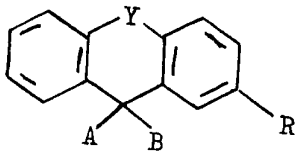


R^1	R^2	R^3	R^4	Melting point, °C
Phenyl	Phenyl	Phenyl	H	226-227
p-Toluene	Phenyl	Phenyl	H	128
o-Chlorophenyl	Phenyl	Phenyl	H	140
m-Trifluoromethylphenyl	Phenyl	Phenyl	H	156
p-Nitrophenyl	Phenyl	Phenyl	H	160-170
p-Chlorophenyl	m-Fluorophenyl	Phenyl	H	116
4-Methylphenyl	2-Pyridyl	Phenyl	H	144-145
2-Ethoxyphenyl	2-Pyridyl	Phenyl	H	123-125
4-Chlorophenyl	2-Pyridyl	4-Fluorophenyl	H	138
Phenyl	4-Pyridyl	Phenyl	CH_3	175-178
Phenyl	4-Pyridyl	Phenyl	H	217-218
Phenyl	4-Pyridyl	Phenyl	H	186-200 lactate
4-Chlorophenyl	Phenyl	1-Imidazolyl	H	140

Continuation of Table 1

R^1	R^2	R^3	R^4	Melting point, °C
2-Fluorophenyl	4-Fluorophenyl	1-Imidazolyl	H	129
4-Fluorophenyl	4-Nitrophenyl	1-Imidazolyl	H	198
Phenyl	Phenyl	1-(2-Methyl)-imidazolyl	CH_3	193
4-Bromophenyl	Phenyl	1-(2-Ethyl)-imidazolyl	C_2H_5	128
4-Chlorophenyl	4-Chlorophenyl	1-(2-Methyl)-imidazolyl	CH_3	220
2,3-Dichlorophenyl	Phenyl	Phenyl	H	128
2-Methyl-4-chlorophenyl	Phenyl	Phenyl	H	158-162
2-Chlorophenyl	Phenyl	2-Chlorophenyl	H	180
3,4-Dimethylphenyl	Phenyl	2-Pyridyl	H	96
2,6-Dimethylphenyl	Phenyl	2-Pyridyl	H	120 hydrochloride
2,3-Dimethylphenyl	Phenyl	4-Pyridyl	H	154

Table 2

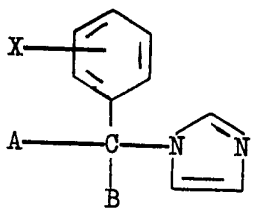


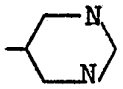
A	B	R	Y	Melting point, °C
Phenyl	1-Imidazolyl	H	-	197-199
4-Bromophenyl	1-Imidazolyl	H	-	181-184
4-Chlorophenyl	1-Imidazolyl	H	$-(CH_2)_2-$	216-218
Phenyl	1-Imidazolyl	H	-O-	160-162
Phenyl	1-Imidazolyl	H	-S-	179-181
Phenyl	1-Imidazolyl	H	-CH=CH-	208-211
3-Pyridyl	1-Imidazolyl	H	-	80-85
3-Pyridyl	1-Imidazolyl	H	$-(CH_2)_2-$	147-149
4-Fluorophenyl	1-Imidazolyl	H	$-(CH_2)_2-$	Salicylate, 137-138
4-Methylthiophenyl	1-Imidazolyl	H	-	Hydrochloride, from 90 onwards (decomposition)
$-COOCH_3$	1-Imidazolyl	H	-	150
$-COOCH_3$	1-Imidazolyl	Cl	-	205-210 (decomposition)
$-COOC_3H_7(n)$	1-Imidazolyl	H	-	85

Continuation of Table 2

A	B	R	Y	Melting point, °C
$-COOCH_3$	1-(1,2,4-Triazolyl)	H	-	140-145
$-COOC_2H_5$	1-(1,2,4-Triazolyl)	H	-	133
$-COOCH_3$	1-(1,2,4-Triazolyl)	Cl	-	90 (decomposition)
$-COOC_4H_9$	1-Imidazolyl	H	-	Hydrochloride, 158 (decomposition)
$-CH_3$	1-Imidazolyl	H	-	139
$-CH(CH_3)_2$	1-Imidazolyl	H	-	125
$-C_2H_5$	1-Imidazolyl	Cl	-	Hydrochloride, 215
$-CH_3$	1-Imidazolyl	Cl	-	130
$-CH_3$	1-Imidazolyl	H	$-CH=CH-$	188
$-CH_2-CH=CH_2$	1-Imidazolyl	H	$-CH_2-CH_2-$	Hydrochloride, 168

Table 3



A	B	X	Melting point, °C
4-Pyridyl	Cyclohexyl	H	90
Phenyl	t-Butyl	4-Cl	137
4-Chlorophenyl	t-Butyl	4-Cl	Hydrochloride, 196
Phenyl	Allyl	H	80
Phenyl	t-Butyl	2,5-$(CH_3)_2$	112
Phenyl	Cyclopropyl	3-CH_3	Hydrochloride, 136
4-Methylphenyl	1-Methylcyclohexyl	4-CH_3	151
Phenyl	t-Butyl	3-CH_3, 4-Cl	95
Phenyl	2-Thienyl	4-F	144-145
Phenyl	3-(5-Methyl)-isoxazolyl	3-CF_3	69
Phenyl	2-(1-Methyl)-imidazolyl	H	200
Phenyl	5-(3,4-Dichloro)-isothiazolyl	4-F	95
Phenyl		H	209

Continuation of Table 3

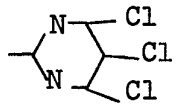
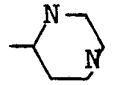
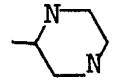
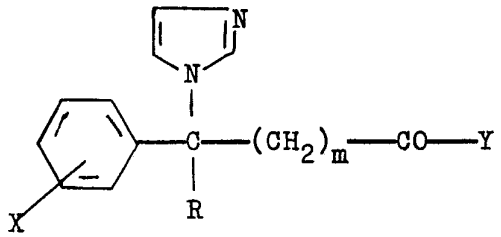
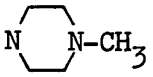
A	B	X	Melting point, °C
Phenyl		H	142-146
Phenyl		H	198
4-Fluorophenyl		H	Hydrochloride, 86

Table 4

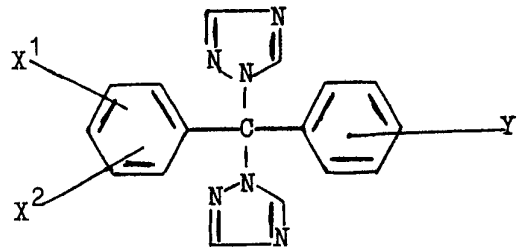


R	X	Y	m	Melting point, °C
Phenyl	H	OCH_3	0	155
Phenyl	H	OCH_3	0	Sulphate, 145
2-Methylphenyl	H	OCH_3	0	148
Phenyl	H	$OC_{10}H_{21}$	0	48
Phenyl	H	$NH(CH_3)_2$	0	202
Phenyl	H		0	Hydrochloride, 118
Phenyl	H		0	173
4-Chlorophenyl	4-Cl	OCH_3	0	132
4-Methoxyphenyl	4-OCH_3	OCH_3	0	131
Phenyl	H	OC_2H_5	1	75

Continuation of Table 4

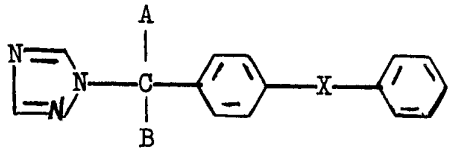
R	X	Y	m	Melting point, °C
$CH(CH_3)_2$	H	OC_2H_5	1	Hydrochloride, 194
Phenyl	H	CH_3	0	103
4-Chlorophenyl	H	Phenyl	0	136
3-Methylphenyl	H	Phenyl	0	120

Table 5



X^1	X^2	Y	Melting point, °C
H	H	H	210
H	2-Cl	H	205
H	4-F	4-CN	75
$3-NO_2$	4-Cl	H	84
5-Cl	2-Cl	H	125

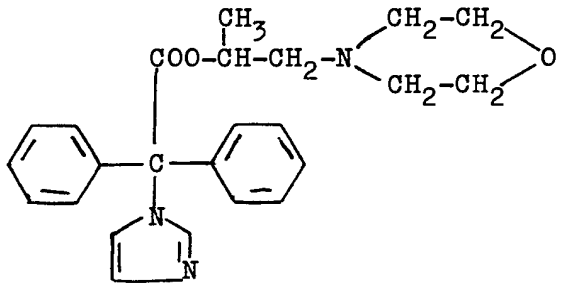
Table 6

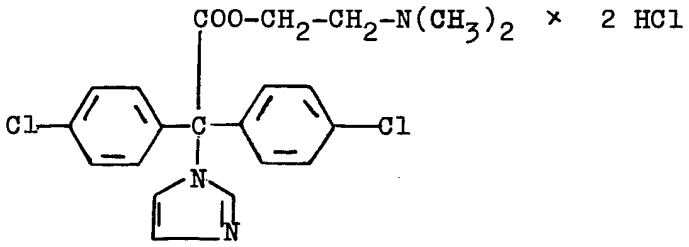


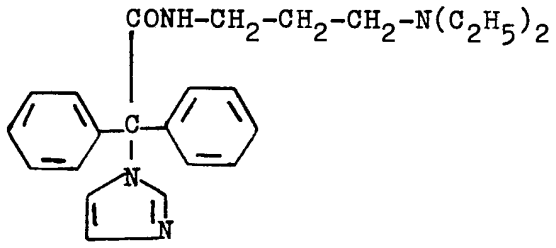
E	A	B	X	Melting point, °C
CH	Phenyl	Phenyl	-	173
CH	2'-(N'-Methylimidazolyl)	Phenyl	-	134
CH	Phenyl	Phenyl	-S-	162-164
CH	Phenyl	Phenyl	-CO-	131-135
CH	Phenyl	Phenyl	-O-	141-144
CH	1,5-Dimethylpyrazol-3-yl	Phenyl	-O-	60
CH	4-Chlorophenyl	4-Chlorophenyl	-O-	136
N	Phenyl	Phenyl	-S-	137-139
N	2'-(N'-Methylimidazolyl)	Phenyl	-	135

Table 7

Phenylazolyl-fatty acid derivatives







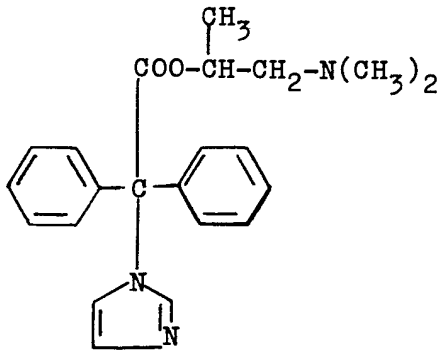
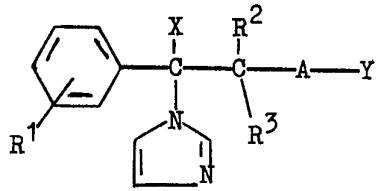


Table 8

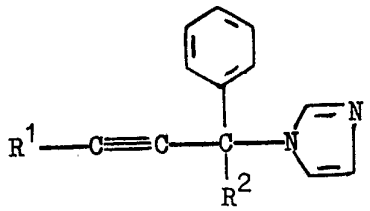


X	Y	R^1	R^2	R^3	A	Melting point, °C
Phenyl	H	H	H	H	-O-	144
Phenyl	CH_3-CH_2-CO-	H	H	H	-O-	74
Phenyl	Cl-C$_6$H$_4$-CO-	H	H	H	-O-	128
Phenyl	$(NO_2)_2$-C$_6$H$_3$-CO-	H	H	H	-O-	132
Phenyl	C$_6$H$_5$-CH=CH-CO-	H	H	H	-O-	87
Phenyl	CH_3-SO_2-	H	H	H	-O-	187
Phenyl	CH_3-C$_6$H$_4$-$SO_2NH-CO-$	H	H	H	-O-	148
Phenyl	$CH_3-NHCO-N(CH_3)-CO-$	H	H	H	-O-	140
Phenyl	C$_6$H$_4$	4-Cl	H	H	-O-	138
Phenyl	Cl-C$_6$H$_4$	H	CH_3	CH_3	-O-	148
Phenyl	H	H	CH_3	H	-O-	154

Continuation of Table 8

X	Y	R^1	R^2	R^3	A	Melting point, °C
Phenyl	H	H		H	-O-	203
$-C(CH_3)_3$	H	H	H	H	-O-	130
$-C(CH_3)_3$	CH_3-CO-	H	H	H	-O-	70
Phenyl	Cl- 	H	H	H	-S-	126
Phenyl	Cl- 	H	H	H	$-SO_2-$	x CH_3COOH 134
Phenyl	CH_3-CO-	H	H	H	-NH-	173

Table 9



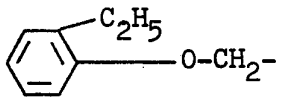
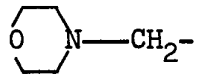
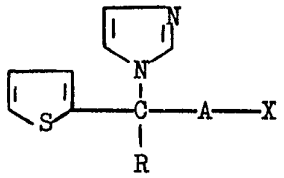
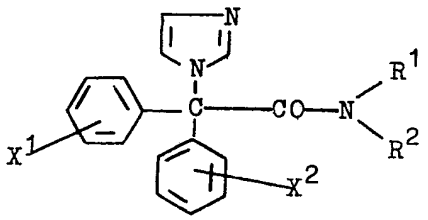
R^1	R^2	Melting point, °C
Phenyl	Phenyl	103-104
Phenyl	4-Chlorophenyl	87-87.5
Phenyl	3-Nitrophenyl	44-46
Phenyl	$C(CH_3)_3$	Oil, n_D^{25} 1.6019
H	Phenyl	136
$CH_3-(CH_2)_4-$	Phenyl	Oil, n_D^{25} 1.5755
	CH_3	Oil, n_D^{25} 1.5852
	Phenyl	63-64
$(C_2H_5)_2N-CH_2-$	Phenyl	83-84

Table 10



R	A	X	Melting point, °C
Thienyl	-CO-	$-OCH_3$	117
Phenyl	$-CH_2-$	-CN	Hydrochloride, 82
4-Chlorophenyl	$-CH_2-$	$-CON(CH_3)_2$	161
Thienyl	-CO-	$-O-CHCH_3-CH_2-N(CH_3)_2$	Oil

Table 11



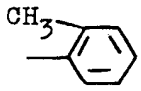
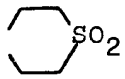
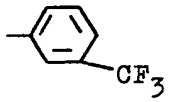
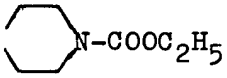
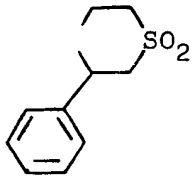
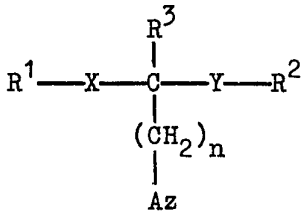
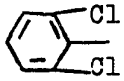
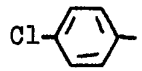
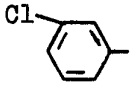
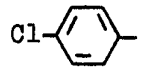
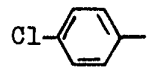
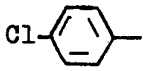
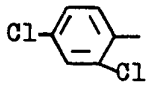
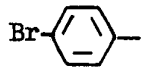
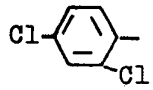
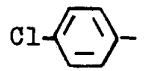
X^1	X^2	R^1	R^2	Melting point, °C
H	H		H	141-143
4-Cl	4-Cl			159-163
H	H		H	219-220
H	H		H	166-168
H	H			156-158
H	H			103-104

Table 12

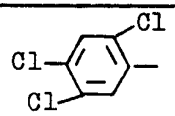
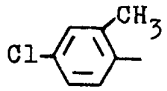
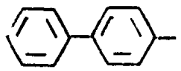
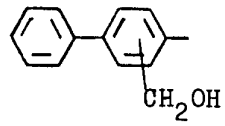
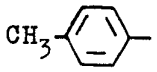
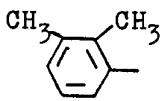
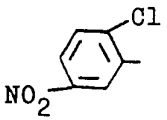


Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-Imidazolyl	0	-O-	-CO-			H	218
1-Imidazolyl	0	-O-	-CO-		$-C(CH_3)_3$	H	135
1-Imidazolyl	0	-O-	$-C(OH)_2-$			H	Hydrochloride, 124
1-Imidazolyl	0	-O-	-CO-			CH_3	Oil
1-Imidazolyl	0	-S-	-CO-		$-C(CH_3)_3$	H	Oil

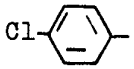
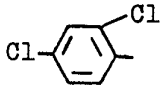
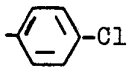
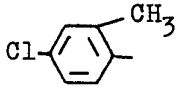
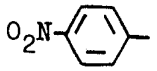
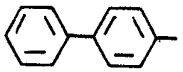
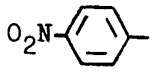
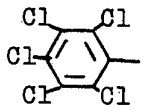
Continuation of Table 12

Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-Imidazolyl	0	-O-	-CO-		$-C(CH_3)_3$		98-102
1-Imidazolyl	0	-O-	$-C(OH)_2-$			H	Hydrochloride, 155
1-Imidazolyl	0	-O-	-CO-				126
1-Imidazolyl	0	-O-	-CO-		$-C(CH_3)_3$	H	106
1-Imidazolyl	0	-O-	-CO-		$-C(CH_3)_3$		Hydrochloride, 208
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	Hydrochloride, 127
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	102-106

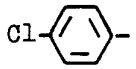
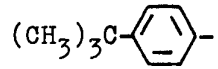
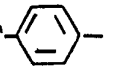
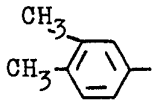
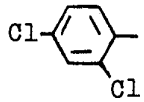
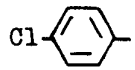
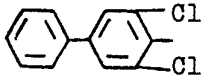
Continuation of Table 12

Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	Hydrochloride, 180-183
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	Hydrochloride, 147-150
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	111-112
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	105-107
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	Hydrochloride, 135
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	Hydrochloride, 143-147
1-Imidazolyl	1	-O-	-CO-		$-C(CH_3)_3$	H	122-123

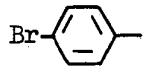
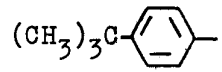
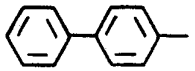
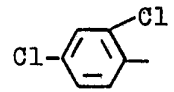
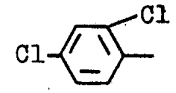
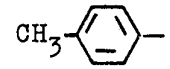
Continuation of Table 12

Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-Imidazolyl	1	-O-	-CO-			H	Hydrochloride, 148-150
1-(1,2,4-Triazolyl)	0	-O-	-CO-			H	101-104
1-(1,2,4-Triazolyl)	0	-O-	-CO-		$-C(CH_3)_3$	H	94-96
1-(1,2,4-Triazolyl)	0	-O-	-CO-		$-C(CH_3)_3$	H	145
1-(1,2,4-Triazolyl)	0	-O-	-CO-		$-C(CH_3)_3$	H	105-106
1-(1,2,4-Triazolyl)	0	-O-	>C=NOH		$-C(CH_3)_3$	H	187
1-(1,2,4-Triazolyl)	0	-O-	$C(OH)_2$		$-C(CH_3)_3$	H	206-207

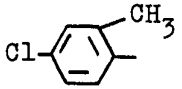
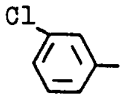
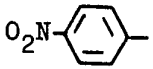
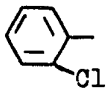
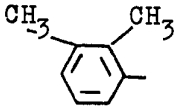
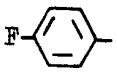
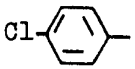
Continuation of Table 12

Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-(1,2,4-Triazolyl)	0	-O-	-CO-		$-C(CH_3)_3$	H	Sulphate, 141
1-(1,2,4-Triazolyl)	0	-	-CO-		$-C(CH_3)_3$		99
1-(1,2,4-Triazolyl)	0	-O-	-CHOH-		$-C(CH_3)_3$	H	113-117
1-(1,2,4-Triazolyl)	0	-O-	-CHOH-		$-C(CH_3)_3$	H	99-110
1-(1,2,4-Triazolyl)	0	-O-	-CHOH-		$-C(CH_3)_3$	H	133-135
1-(1,2,4-Triazolyl)	0	-O-	$-CCH_3OH-$		$-C(CH_3)_3$	H	101-103
1-(1,2,4-Triazolyl)	0	-O-	$-CCH_3OH-$			H	171-173
1-(1,2,4-Triazolyl)	0	-O-	-CHOH		$-C(CH_3)_3$	H	142-144

Continuation of Table 12

Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-Imidazolyl	0	-O-	-CHOH		$-C(CH_3)_3$	H	145-147
1-Imidazolyl	0	-O-	-CHOH-		$-C(CH_3)_3$	H	173-174
1-Imidazolyl	0	-O-	-CHOH		$-C(CH_3)_3$	H	145-150
1-Imidazolyl	0	-O-	-CHOH-		$-C(CH_3)_3$	H	136-148
1-Imidazolyl	0	-O-	-CHOH-		$-C(CH_3)_3$	H	Hydrochloride, 190-210
1-Imidazolyl	0	-O-	-CHOH-		$-C(CH_3)_3$		159-160
1-(1,2,4-Triazolyl)	1	-O-	-CO-		$-C(CH_3)_3$	H	42-44

Continuation of Table 12

Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-(1,2,4-Triazolyl)	1	-O-	-CO-		$-C(CH_3)_3$	H	63-65
1-(1,2,4-Triazolyl)	1	-O-	-CO-		$-C(CH_3)_3$	H	73-74
1-(1,2,4-Triazolyl)	1	-O-	-CO-		$-C(CH_3)_3$	H	97-98
1-(1,2,4-Triazolyl)	1	-O-	-CHOH-		$-C(CH_3)_3$	H	106-108
1-(1,2,4-Triazolyl)	1	-O-	-CHOH-		$-C(CH_3)_3$	H	132-134
1-(1,2,4-Triazolyl)	1	-O-	-CHOH-		$-C(CH_3)_3$	H	121-122
1-(1,2,4-Triazolyl)	1	-O-	$-CCH_3OH-$		$-C(CH_3)_3$	H	150

Continuation of Table 12

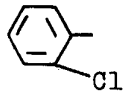
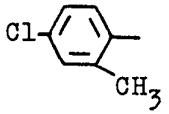
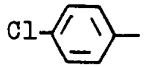
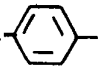
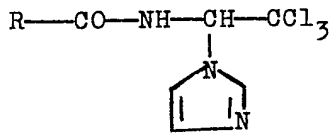
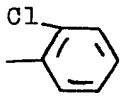
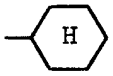
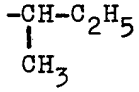
Az	n	X	Y	R^1	R^2	R^3	Melting point, °C
1-Imidazolyl	1	-O-	-CHOH-		$-C(CH_3)_3$	H	162-163
1-Imidazolyl	1	-O-	-CHOH-		$-C(CH_3)_3$	H	163-164
1-Imidazolyl	1	-O-	$-CCH_3OH-$		$-C(CH_3)_3$	H	155
1-Imidazolyl	1	-O-	$-C(CH_2-C_6H_5)OH$		$-C(CH_3)_3$	H	179-181

Table 13



R	Melting point, °C
H	110-112
$-C(CH_3)_3$	114-118
	152-154
	170-171
	156-158

The active compounds used according to the invention exhibit a powerful action against Pityrosporum ovale. Pityrosporum ovale is a blastomycete which is only parasitic in the uppermost layers of human skin, particularly in excessively greasy skin. It is regarded as the cause of the following changes in skin, which are *not* regarded as skin diseases: 1) Pityriasis simplex, 2) Pityriasis oleosa and 3) Pityriasis circinata. It is also regarded as the cause of the following, which are considered to be skin diseases: seborrhoeic dermatitis and Acne vulgaris (as a coexistent germ).

All the skin changes caused, or partially caused, by Pityrosporum ovale are grouped under the generic term "seborrhoea".

Other coexistent germs found in seborrhoea are: Staph. albus and corynebacteria, as well as Malassezia furfur. The latter are also known as the pathogens of erythrasma and of Pityriasis versicolor.

Seborrhoea is widespread and is frequently one of the causes of loss of hair and formation of scaly skin, especially on the scalp.

Seborrhoeic eczemas also occur very frequently on the face and are therefore objectionable and disturbing. The invention particularly provides a process for combating skin changes caused wholly or partially by *Pityrosporum ovale* which comprises applying to the skin a compound of the formula (I).

Pityrosporum ovale was cultured and the MIC determinations were carried out with a large number of azole derivatives. The growth of Pityrosporum ovale is considerably slower than, for example, of species of Candida or Torulopsis—it takes 3 to 5 days. It requires Abbe's medium as a special nutrient medium.

Procedure:

1.) Setting up the dilution series of each preparation: 6.4 mg of preparation are dissolved in 1 ml of analytical grade dimethylformamide and 9 ml of distilled water are added. 1 ml now contains 640 mcg (640 microgrammes) of preparation. If 2 ml are withdrawn and added to 2 ml of H_2O, the resulting concentration is 320 mcg/

ml. If this is continued progressively, the following dilution series, in mcg/ml, is obtained: 640 — 320 — 160 — 80 — 40 — 20 — 10 — 5 — 2.5 — 1.25 — 0.625 — 0.313 — 0.156 — 0.078 — 0.039 — 0.02 — 0.01.

2.) Charging the test tubes: 0.5 ml portions of the particular dilution are introduced into test tubes.

3.) Charging with nutrient medium: Abbe's medium is used.

Recipe:

15.0 g of malt extract (Messrs. Diamalt)
+ 2.5 g of peptone (Messrs. BBL)
+ 10.0 g of ox bile (Messrs Merck)
+ 20.0 g of agar-agar (Messrs. Difco)
+ 100.0 g of Tween 40 mixture*) (TWEEN and DIFCO are Trade Marks)
+ 900.0 g of distilled water.

200 ml portions of Abbe's medium are introduced into nutrient medium flasks. For use, the previously calculated amount of Abbe's medium is liquefied in a steaming pot and cooled until only warm to the touch; 4.5 ml are then added to each test tube. A second person receives each test tube and twirls it between his hands, like a kitchen whisk. This achieves good mixing of the diluted preparation with the nutrient medium. Each test tube is then immediately brought into a slanting position, in the same way as is usually employed to prepare agar slants.

The final concentrations of the various preparations are then, in mcg/ml of test medium: 64 — 32 — 16 — 8 — 4 — 2 — 1 — 0.5 — 0.25 — 0.125 — 0.062 — 0.031 — 0.016 — 0.008 — 0.004 — 0.002 — 0.001.

The culture control and the nutrient medium control are each 1 test tube in which 0.5 ml of H_2O is introduced in place of the preparation.

4.) Inoculation with Pityrosporum ovale:

We used a culture which had been grown for 3 weeks in Benham's fluid medium at 28°C.

Recipe for Benham's fluid medium:

1.0 g of KH_2PO_4
0.5 g of $MgSO_4.7H_2O$
1.25 g of asparagine
500 ml of distilled water
500 ml of 4% strength Tween 80 in H_2O

bring to pH 6.4 with NaOH.

After the nutrient medium has solidified thoroughly in all the test tubes, 0.1 ml of culture is allowed to run over each slant, except for the test tube of the nutrient medium control. 0.1 ml of physiological NaCl solution is added to the latter.

5.) Incubation and readings:

The incubation is carried out at 28°C. After 3 days, the culture control test tubes show germ growth, which reaches an optimum after 5 days.

The MIC = minimum inhibitory concentration, and the PI = partial inhibition (retardation of growth by about 90% relative to the control, that is to say only about 10% of the germs have grown) are read off in comparison to the control.

Of course, all the work must—as is usual in microbiology—be carried out under sterile conditions, that is to say, using, for example, sterile test tubes, pipettes, nutrient media and the like.

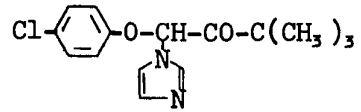
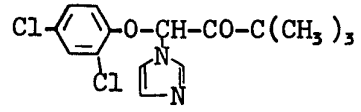
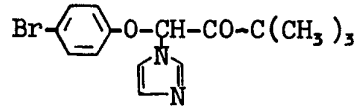
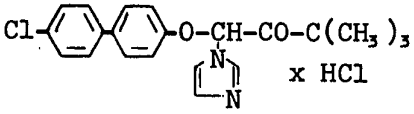
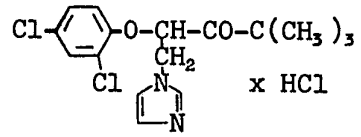
Table 14 which follows lists the MIC values = minimum inhibitory concentrations, and PI values = partial inhibitions of a representative selection of the azole antimycotics claimed.

According to these results, the active compounds according to the invention can very justifiably be used in combination with dermatologically acceptable carriers comprising detergent active compounds and/or perfumes to form hair and skin toiletry compositions particularly since the azole group is also active against Staph. albus and corynebacteria at orders of magnitude of 2 mcg/ml.

*) Tween mixture: 100 ml of Tween 40 (Messrs. Merck) + 400 ml of distilled water + 25 g of highest purity glycerol (Messrs. Merck) are mixed and then made up to 1,000 ml with distilled water.

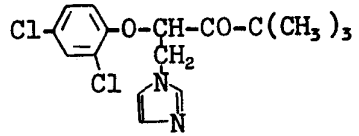
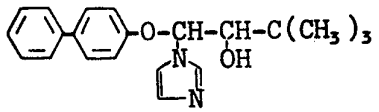
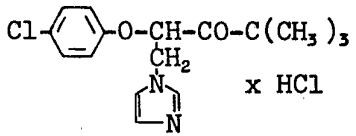
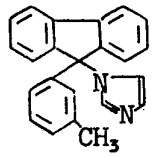
Table 14:

MIC and PI values of Pityrosporum ovale in the presence of various azole derivatives

Compound (Example No.)	Reading after 3 days		Reading after 5 days	
	MIC mcg/ml	PI* mcg/ml	MIC mcg/ml	PI* mcg/ml
(1) 	<1		<1	
(2) 	<1		<1	
(3) 	<1		<1	
(4)  x HCl	<1		<1	
(5)  x HCl	2	<1	2	<1

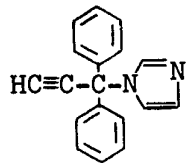
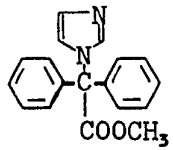
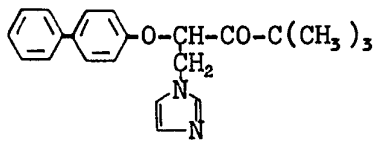
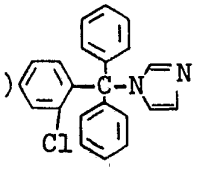
Continuation of Table 14

MIC and PI values of Pityrosporum ovale in the presence of various azole derivatives

Compound (Example No.)	Reading after 3 days		Reading after 5 days	
	MIC mcg/ml	PI* mcg/ml	MIC mcg/ml	PI* mcg/ml
(6) 	2	< 1	2	< 1
(7) 	4	2	8	2
(8)  x HCl	4	2	8	4
(9) 	8	2	8	4

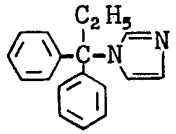
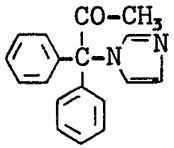
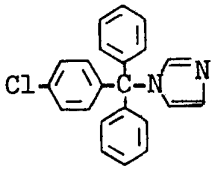
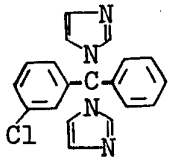
Continuation of Table 14

MIC and PI values of Pityrosporum ovale in the presence of various azole derivatives

Compound (Example No.)	Reading after 3 days MIC mcg/ml	Reading after 3 days PI* mcg/ml	Reading after 5 days MIC mcg/ml	Reading after 5 days PI* mcg/ml
(10) 	8	<1	16	<1
(11) 	16	<1	16	<1
(12) 	8	<1	8	<1
(13) 	16	8	16	8

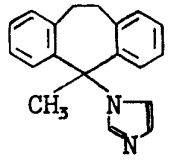
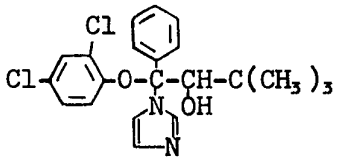
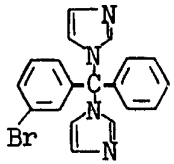
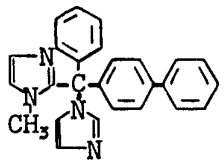
Continuation of Table 14

MIC and PI values of Pityrosporum ovale in the presence of various azole derivatives

Compound (Example No.)	Reading after 3 days		Reading after 5 days	
	MIC mcg/ml	PI* mcg/ml	MIC mcg/ml	PI* mcg/ml
(14) 	32	4	32	4
(15) 	32	4	64	4
(16) 	>64	16	>64	16
(17) 	>64	32	>64	32

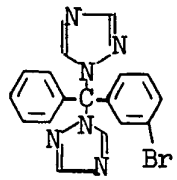
Continuation of Table 14

MIC and PI values of Pityrosporum ovale in the presence of various azole derivatives

Compound (Example No.)	Reading after 3 days		Reading after 5 days	
	MIC mcg/ml	PI* mcg/ml	MIC mcg/ml	PI* mcg/ml
(18) 	>64	32	>64	32
(19) 	>64	64	>64	64
(20) 	>64	64	>64	64
(21) 	>64		>64	

Continuation of Table 14

MIC and PI values of Pityrosporum ovale in the presence of various azole derivatives

Compound (Example No.)	Reading after 3 days		Reading after 5 days	
	MIC mcg/ml	PI* mcg/ml	MIC mcg/ml	PI* mcg/ml
(22) 	>64		>64	

+ Partial inhibition was recorded if the growth of the cultures was reduced by at least 90% compared to the control.

The active compounds according to the invention can be used in many diverse cosmetic preparations. The following hair toiletries and hairdressing preparations may be mentioned as examples of hair toiletry compositions of the invention: hair soaps, hair creams, hair lotions, hair tonics, hair oils, hair pomades, hair brilliantines and especially hair rinses and shampoos. The following may be mentioned as skin toiletry compositions of the invention: soaps, fluid creams and skin gels, skin oils, skin function oils, face lotions, astringents and deodorants.

If the active compound preparations are shampoos, these may be a clear liquid, opaque liquid, gel, cream or powder.

In any interaction of the shampoos with the hair and skin or scalp a decisive factor is whether the detergent-active compounds on which the shampoos are based are anionic or cationic or non-ionic surfactants or whether they are combinations of these substances.

The following may be mentioned as examples of such anionic detergent-active substances: C_{10}—C_{20}-alkyl-carboxylates and alkylene-carboxylates, alkyl-ether-carboxylates, fatty alcohol sulphates, fatty alcohol-ether sulphates, alkylolamide-sulphates and alkylolamide-sulphonates, fatty acid alkylolamide-polyglycol ether

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sulphates, alkanesulphonates and hydroxyalkanesulphonates, olefinesulphonates, acyl esters of isothionates, α-sulpho-fatty acid esters, alkylbenzenesulphonates, alkylphenol glycol ether-sulphonates, sulphosuccinates, sulphosuccinic acid half-esters and diesters, fatty alcohol-ether phosphates, albumen-fatty acid condensation products, alkyl monoglyceride sulphates and sulphonates, alkyl glyceride-ether sulphonates, fatty acid methyltaurides, fatty acid sarcosinates and sulphoricioleates. These compounds and their mixtures are used in the form of their water-soluble or water-dispersible salts, for example the sodium, potassium, magnesium, ammonium, monoethanolammonium, diethanolammonium and triethanolammonium and analogous alkylolammonium salts.

Suitable cationic detergent-active compounds are, for example, quaternary ammonium salts such as di-(C_{10}—C_{24}-alkyl)-dimethylammonium chloride or bromide, preferably di-(C_{12}—C_{18}-alkyl)-dimethylammonium chloride or bromide; C_{10}—C_{24}-alkyl-dimethylethylammonium chloride or bromide; C_{10}—C_{24}-alkyl-trimethylammonium chloride or bromide, preferably cetyl-trimethylammonium chloride or bromide and C_{20}—C_{22}-alkyl-trimethylammonium chloride or bromide; C_{10}—C_{24}-alkyl-dimethyl-benzylammonium chloride or bromide, preferably C_{12}—C_{18}-alkyl-dimethyl-benzylammonium chloride; N-(C_{10}—C_{18}-alkyl)-pyridinium chloride or bromide, preferably N-(C_{12}—C_{16}-alkyl)-pyridinium chloride or bromide; N-(C_{10}—C_{18}-alkyl)-isoquinolinium chloride, bromide or monoalkyl-sulphate; N-(C_{12}—C_{18}-alkylolcolaminoformylmethyl)-pyridinium chloride; N-(C_{12}—C_{18}-alkyl)-N-methyl-morpholinium chloride, bromide or monoalkyl-sulphate; N-(C_{12}—C_{18}-alkyl)-N-ethyl-morpholinium chloride, bromide or monoalkyl-sulphate; C_{16}—C_{18}-alkyl-pentaoxethyl-ammonium chloride; diisobutyl-phenoxyethyoxyethyldimethylbenzylammonium chloride; salts of N,N-diethyl-aminoethyl-stearylamide and -oleylamide with hydrochloric acid, acetic acid, lactic acid, citric acid and phosphoric acid; N-acylamidoethyl-N,N-diethyl-N-methylammonium chloride, bromide or monoalkyl-sulphate and N-acylamidoethyl-N,N-diethyl-N-benzylammonium chloride, bromide or monoalkyl-sulphonate, wherein acyl is preferably stearyl or oleyl.

Non-ionic detergent active compounds can only be used with adjuvants since they have a low foaming power. They include lyophilic higher-molecular esters of aliphatic polyhydric alcohols with aliphatic polycarboxylic acids, and polyglycol esters of fatty acids. The following may be mentioned as individual examples: fatty alcohol ethoxylates (alkyl-polyethylene glycols); alkylphenol-polyethylene glycols; alkylmercaptan-polyethylene glycols; fatty amine ethoxylates (alkylamine-polyethylene glycols); fatty acid ethoxylates (acyl-polyethylene glycols); polypropylene glycol ethoxylates (trade mark: Pluronic); fatty acid alkylolamides (fatty acid amide-polyethylene glycols); sucrose esters; sorbitol esters and polyglycol ethers.

Examples of amphoteric surfactants which can be added to the shampoos are: N-(C_{12}—C_{18}-alkyl)-β-aminopropionates and N-(C_{12}—C_{18}-alkyl)-β-iminodipropionates as alkali metal salts and mono-, di- and tri-alkylol-ammonium salts; N-acyl-amidoalkyl-N,N-dimethyl-acetobetaine, preferably N-(C_8—C_{18}-acyl)-amidopropyl-N,N-dimethyl-acetobetaine; C_{12}—C_{18}-alkyl-dimethyl-sulphopropyl-betaine; amphoteric surfactants based on imidazoline (trade marks: Miranol, Steinapon, preferably the sodium salt of 1-(β-carboxy-methyloxethyl)-1-(carboxy-methyl)-2-lauryl-imidazolinium; amine oxides, for example C_{12}—C_{18}-alkyl-dimethylamine oxide and fatty acid amido-alkyl-dimethylamine oxide.

The preparations according to the invention can, in addition to detergent-active compounds and/or perfumes contain other additives customary in cosmetics, for example, dyestuffs, including those which at the same time dye or tint the hair, solvents, opacifying agents or pearlescent agents, for example esters of fatty acids with polyols, magnesium salts and zinc salts of fatty acids, dispersions based on copolymers, thickeners such as sodium chloride, potassium chloride, ammonium chloride and sodium sulphate, fatty acid alkylolamides, cellulose derivatives, natural gums, plant extracts, albumen derivatives, collagen derivatives such as gelatine, collagen hydrolysis products, natural or synthetic polypeptides, egg yolk, lecithin, lanolin and lanolin derivatives, fats, oils, fatty alcohols, silicones, deodorants, anti-microbial substances, other anti-seborrhoeic substances, materials having a keratolytic and keratoplastic action such as, for example, sulphur, salicylic acid and enzymes.

The abovementioned cationic surfactants can also be present in other preparations, such as, for example, in hair rinses, hair tonics and hair regenerating agents and in anhydrous oily preparations, such as hair oil, hair pomade and hair

brilliantine. The preparations of the antimycotically active azole derivatives can also be offered in the form of aqueous and aqueous-alcoholic hair lotions, wave-setting lotions (hair fixatives), including such preparations in the form of gels, and in the form of aerosols as hair sprays as well as in the form of hair toiletry creams and gels and hairdressing creams and gels.

Ethanol and isopropanol are preferentially employed as alcohols.

These and all preparations already mentioned previously are produced in a manner which is in itself known by bringing together the individual components, with addition of the active compounds according to the invention, and further processing the mixture appropriately to the type of preparation concerned.

The various cosmetic preparations containing the active compounds according to the invention can be used in the customary manner, preferably by rubbing or massaging into the scalp.

The active compounds according to the invention, especially the compounds (1) to (8) in Table 14, can preferably be present in the various preparations in concentrations of between 0.1 to 1%. Within this range, the concentrations of the special preparations depend on their intended use. Certain preparations, such as, for example, concentrates which have to be diluted before use, may also contain higher concentrations.

The following preparations may be mentioned by way of examples:

Example A: Shampoo (liquid).

Sodium lauryl ether sulphate	50.0%
Coconut oil fatty acid diethanolamide	5.0%
Water	44.0%
Azole antimycotic of formula (I)	1.0%
Preservative, dyestuff, perfume	q.s.

Example B: Shampoo (liquid).

Monoethanol ammonium lauryl sulphate	50.0%
Oleic acid diethanolamide	3.5%
Water	45.5%
Azole antimycotic of formula (I)	1.0%
Preservative, dyestuff, perfume	q.s.

Example C: Shampoo (cream).

Sodium salt of the condensation product of saturated fatty acids of medium chain length and methyltaurine (approx. 30% content of active substance)	70.0%
Sodium salt of the condensation product of higher-molecular saturated fatty acids and methyllaurine (approx. 30% content of active substance)	15.0%
Fatty acid polyglycol ester (as an opacifying agent)	3.0%
Sodium salt of the condensation product of saturated fatty acids of average chain length and sarcosine (approx. 65% content of active substance)	3.0%

EXAMPLE cont'd.

Water	8.0%
Azole antimycotic of formula (I)	1.0%
Preservative, dyestuff, perfume	q.s.

Example D: Shampoo (in aerosol form).

Sodium lauryl-ether-sulphate (27—28% content of active substance)	55.0%
Sodium lauryl-sulphate (>90% content of active substance)	5.0%
Coconut fatty acid diethanolamide	3.0%
Azole antimycotic of formula (I)	1.0%
Water	36.0%
Preservative, dyestuff, perfume	q.s.

Packaged as: 92% of the shampoo of the above composition and 8% of a propellant mixture of dichlorodifluoromethane/1,1,2,2-tetrafluorodichloroethane (40:60)

Example E: Shampoo (powder).

Sodium oleyl-methyltauride (approx. 64% content of active substance)	32.0%
Sodium tripolyphosphate or sodium hexametaphosphate	3.0%
Dried sodium sulphate	64.0%
Azole antimycotic of formula (I)	1.0%
Anti-caking agent, for example calcium stearate or highly disperse amorphous silica or products based on $CaO/P_2O_5/SiO_2$, perfume oil and dyestuff	q.s.

Example F: Hair lotion.

Isopropanol	50.0%
Vitamin H	0.2%
Diisopropyl adipate	1.0%
Perfume oil H + R	1.0%
Water	47.0%
Inositol	0.3%
Azole antimycotic of formula (I)	0.5%

Example G: Hair fixative.

Copolymer of 50 parts of vinyl acetate and 50 parts of N-vinylpyrrolidone (approx. 50% content of active substance in isopropanol solution)	6.0%
Isopropanol	45.0%
Azole antimycotic of formula (I)	0.5%
Pentaoxethyl-stearyl-ammonium chloride (approx. 20% content of active substance)	2.0%
Perfume oil	q.s.
Water	ad 100.0

Example H: Skin oil.

Oleic acid decyl ester	30.00%
Caprylic/capric acid triglyceride	30.00%
1-(4-chlorophenoxy)-1-(1-imidazolyl)-3,3-dimethyl-2-butanone (I)	1.00%
Paraffin, mobile	39.00%

Perfume oil according to requirements

Mix and warm to 90°C until (I) has dissolved. Then stir cold.

Example J. Face solution.

A	Cetyl stearyl alcohol with 12 moles of ethylene oxide	3.00%
	Mixture of mono- and di-glyceride of palmitic and stearic acid	9.00%
	Caprylic/capric acid triglyceride	5.00%
	Paraffin, mobile	3.00%
	Azole antimycotic of Example H.	1.00%
B	Glycerol, anhydrous	8.00%
	Water, demineralised	ad 100.00%

Perfume and preserving agent according to requirements

A: Warm to 85° until antimycotic has dissolved, then cool to 70°

B: Warm to 70°, then emulsify A into B and homogenise

Example K: Cream.

A	Cetyl stearyl alcohol with 12 moles of ethylene oxide	3.00%
	Mixture of mono- and di-glycerides of palmitic and stearic acid	14.00%

EXAMPLE cont'd.

		2-octyldodecanol	20.00%
		Caprylic/capric acid triglyceride	8.00%
		Azole antimycotic of Example H	1.00%
	B	1,2-propylene glycol	5.00%
		Water, demineralised	ad 100.00%

A: Warm to about 80°C until antimycotic has dissolved, then cool to 70°C

B: Warm to 75°C and emulsify A into B

Example L:

	A	Glycerol-sorbitan-fatty acid ester	8.00%
		Paraffin oil, mobile	8.00%
		Caprylic/capric acid triglyceride	20.00%
		Azole Antimycotic of Example H	1.00%
	B	Water, demineralised	ad 100.00%

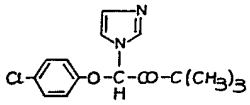
Perfume and preserving agent according to requirements

A: Warm to about 80°C until antimycotic has dissolved, then cool to 70°C.

B: Warm to 75°C, then emulsify into A.

Examples of the preparation of the chemicals.

Example (I).



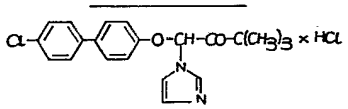
Charge: 15.25 g (0.05 mol) of [1-bromo]-[1-(4'-chloro)-phenoxy]-3-dimethyl-butan-2-one and 12 g (0.18 mol) of imidazole.

The two components are dissolved in 120 ml of acetonitrile and the solution is then heated to the boil under reflux for 18 hours. After distilling off the solvent in vacuo, 150 ml of water are added to the residue and the aqueous phase is then additionally treated three times with 30 ml of water at a time, and dried, and the solvent is distilled off in vacuo. After recrystallising the residue from about 400 ml of ligroin, 10.5 g (72% of theory) of [1-imidazolyl]-[1-(4'-chloro)-phenoxy]-3-dimethyl-butan-2-one of melting point 135°C are obtained.

1-Bromo-[1-(4'-chloro)-phenoxy]-3-dimethyl-butan-2-one used as the starting material, is obtained from 4-chlorophenol and bromopinacolone, followed by bromination with bromine at 140°C (melting point 80°C).

The compounds used in Examples (2) and (3) of Table 14 are prepared analogously.

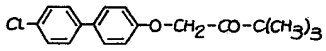
Example (II).



605 g (2 mols) of [1-(4'-(4''-chlorophenyl)-phenoxyl-3,3-dimethyl-butan-2-one are dissolved in 3 l of methylene chloride. 170 ml (2.1 mols) of sulphuryl chloride are added dropwise at 40°C over the course of 2 to 3 hours and the mixture is then stirred for 15 hours at this temperature. Thereafter the solvent is distilled off in vacuo and the residue is dissolved in 1.5 l of methyl ethyl ketone. This solution is added dropwise, with slight cooling, at 20°C, to a suspension of 280 g (4 mols) of imidazole and 280 g (2 mols) of powdered potassium carbonate in 3 l of methyl ethyl ketone. After stirring for 48 hours at room temperature, the solvent is distilled off. The residue is taken up in 3 l of methylene chloride, washed with four times 1 l of water and then dried over sodium sulphate, and the solvent is distilled off in vacuo. The oil which remains is recrystallised from 1 l of diisopropyl ether.

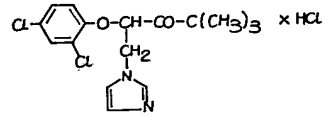
This crude base is dissolved in approx. 1.2 l methylene chloride. 550 ml of approx. 4 N hydrochloric acid in ether are added cautiously and the solvent is then distilled off. 1 l of ethyl acetate is then added to the oil which remains and the mixture is heated, whereupon spontaneous crystallisation occurs. After heating for ½ hour, the crystals are filtered off hot, washed with a little ethyl acetate and dried in vacuo. After two recrystallisations from acetone, 210 g (26% of theory) of [1-imidazolyl-(1)]-[1-(4'-'4''-chlorophenyl)-phenoxy]-3,3-dimethyl-butan-2-one hydrochloride of melting point 148—150°C are obtained.

Starting product.



280 g (2 mols) of powdered potassium carbonate are suspended in 2 l of methyl ethyl ketone. 409 g (2 mols) of 4'-chloro-hydroxybiphenyl are added and the mixture is heated to the boil. Thereafter 260 g (2 mols) of α-chloropinacolone are added dropwise over the course of 1 hour and the mixture is heated under reflux for 15 hours. After cooling, the solid residue is filtered off, washed and recrystallised from ligroin. 513 g (79% of theory) of [1-(4'-(4''-chlorophenyl)-phenoxyl-3,3-dimethyl-butan-2-one of melting point 90°C are obtained.

Example (III).



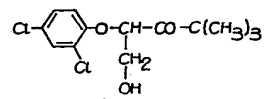
29.1 g (0.1 mol) of 2-(2,4-dichlorophenoxy)-1-hydroxy-4,4-dimethyl-pentan-3-one are taken up in 200 ml of toluene, 10.2 g (0.14 mol) of imidazole are added dropwise thereto and the reaction solution is boiled for 3 hours under a water separator. Thereafter the solvent is distilled off in vacuo, 100 ml of water are added to the oil obtained and the mixture is extracted with twice 100 ml of methylene chloride.

The organic phase is washed with twice 50 ml of water and dried over sodium sulphate, and the solvent is distilled off in vacuo.

An oil is obtained which is taken up in 50 ml of ether, and 50 ml of ether saturated with dry hydrogen chloride are added. The solvent is distilled off in vacuo, the resulting oil is taken up in a mixture of 500 ml of ligroin and 300 ml of ethyl acetate and the mixture is heated to the boil under reflux. After carefully decanting the resulting solution, and cooling it, 18.5 g (49% of theory) of 2-(2,5-dichlorophenoxy)-4,4-dimethyl-1-(1-imidazolyl)-pentan-3-one hydrochloride precipitate as colourless crystals which are isolated by filtration.

Melting point: 118°C.

Starting material.

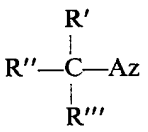


26.1 g (0.1 mol) of 1-(2,4-dichlorophenoxy)-3,3-dimethyl-butan-2-one are

dissolved in 200 ml of ethanol and 20 g (0.24 mol) of 40% strength formaldehyde solution are added, followed by about 5 ml of 10% strength sodium hydroxide solution until the pH is 9. The reaction mixture is heated under reflux for 3 hours and the solvent is distilled off in vacuo. The resulting precipitate is filtered off and rinsed thoroughly with petroleum ether. The filtrate is concentrated in vacuo. An oil consisting of crude 2-(2,4-dichlorophenoxy)-1-hydroxy-4,4-dimethyl-pentan-3-one remains.

WHAT WE CLAIM IS:—

1. A hair or skin toiletry composition comprising at least one azole antimycotic which is active against skin changes wholly or partially caused by *Pityrosporum ovale* and which has the formula (I):—



(I)

wherein Az is an optionally substituted imidazole or triazole group connected to the carbon atom by a nitrogen atom, and

R', R'' and R''' are independently selected from hydrogen atoms, optionally substituted phenyl groups, optionally substituted heterocyclic groups having O, S, or N as a hetero atom, optionally substituted aliphatic groups, optionally substituted alicyclic groups, ester, ether, alkenyl, alkinyl, keto, hydroxy, amido and amino groups or

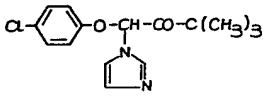
R' and R'' together represent two optionally substituted phenyl groups linked together by a bridging atom or group,

or a salt thereof, dispersed in a dermatologically acceptable carrier which contains a detergent active compound and/or a perfume.

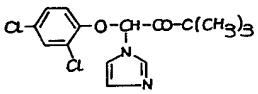
2. A shampoo composition comprising at least one azole antimycotic of the formula (I) and a dermatologically acceptable detergent active compound.

3. A composition according to claim 1 or claim 2 containing at least 30% by weight of the detergent active compound.

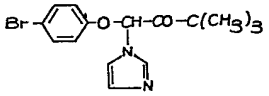
4. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



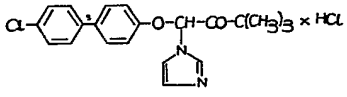
5. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



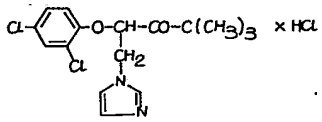
6. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



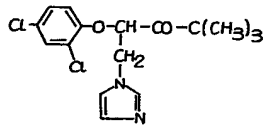
7. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



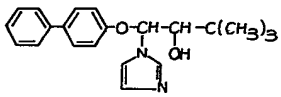
8. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



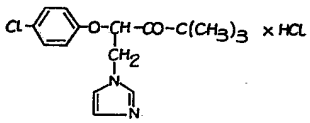
9. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



10. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



11. A composition according to any one of claims 1 to 3 wherein the azole antimycotic is a compound of the formula



12. A composition according to any one of claims 1 to 3 wherein the active ingredient is any of the azole antimycotics specifically disclosed herein in Tables 1 to 13 and Examples 9, 10, 22 in Table 14.

13. A composition according to any one of claims 1 to 12 comprising from 0.05 to 5% by weight of the active ingredient.

14. A composition according to claim 13 comprising from 0.1 to 1.0% by weight of the active ingredient.

15. A composition substantially as hereinbefore described in any one of Examples A to F.

16. A composition substantially as hereinbefore described in any one of Examples H, J and K.

17. A process for combating skin changes wholly or partially caused by *Pityrosporum ovale* which comprises applying to the skin a compound as defined in any one of claims 1 and 3 to 11.

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